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09/784,739	02/14/2001	Surya K. Goli	PF-0162-3 DIV	3353

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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/784,739	GOLI ET AL.
Examiner	**Art Unit**
Ja-Na A Hines	1645

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *1,5-7 and 10-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4 and 8-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/14/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the examiner would not be subject to any undue burden by considering the claims of Groups I, III, IV and XIII because the determination of novelty for the polynucleotide of group II overlaps with the novelty of transgenic organisms in group III. However, Inventions II and III are related as different products. The products are distinct as claimed because they have different structures and different uses. Group II is drawn to a polynucleotide that has a distinct structure representative of its nucleic acid sequence, which is unlike group III's transgenic organisms. Moreover, the transgenic organism has different uses, different functions, effects and is capable of use without the polynucleotide. Therefore, the products of the inventions are distinct as claimed and the scope of search does not overlap in such a way as to prevent an undue burden on the examiner's search.

Applicants argue that the search of Group I would substantially overlap with a search for the invention of group II and that the search of the antibody of group IV would be similarly congruent, thus the examiner's search would be minimal. Applicants submit that a prior art search would encompass a composition comprising an agonist and the associated method.

However, this is not found persuasive because groups II and I, IV and XII are related as different products. The products are distinct as claimed because they have

groups. No search for the antibody, polypeptide or composition is required when searching the polynucleotide of group II. Moreover, an additional undue burden would be placed on the examiner in view of the additional search and considerations associated with inventions of groups I, IV and XII.

It is noted that in view of applicants arguments drawn to serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation of separate classification, or separate status in the art, or a different field of search; A demonstration each of these aspects was set forth in the record in the previous office action. With respect to a different field of search – Because these inventions are distinct and have acquired separate status in the art as shown by their different classification, recognized divergent subject matter and because the search required for each invention is not substantially coextensive with the search required for the remaining invention, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and do **not** represent all the classes and subclasses, which must be searched for each invention; nor is the search limited to issued US patents, but rather includes published foreign patents and applications as well as literature search.

Applicant asserts that the claims of Group V-VII are of a different scope but have already been allowed and therefore there would be no undue burden of search.

However, the fact that the claims have been previously examined does not in itself alleviate the burden of search. The consideration for each patent application is

The requirement is still deemed proper and is therefore made FINAL.

2. Therefore claims 2-4 and 8-9 under consideration in this office action and claims 1, 5-7, 10-24 has been withdrawn from consideration.

Priority

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No.6,248,325" should follow the filing date of the parent application.

Drawings

4. The corrected or substitute drawings were received on February 14, 2001. These drawings are acceptable.

Specification

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the

Claim Objections

6. Claims 2-4 are objected to because of the following informalities: Claim 2 is dependent on non-elected claim 1. In view of their dependence, claims 2-4 have been treated to encompass the components of claim 1, however appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2-4 and 8-9 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 2 is dependent upon claim 1 which is drawn to a purified polypeptide comprising an amino acid sequence selected from a group of amino acid sequences, biologically-active fragments and immunogenic fragments. The written description in this

biologically-active and immunogenic fragments thereof. Neither the specification nor the claims teach how to define biologically-active and immunogenic fragments thereof. Neither the claims nor the specification teach how to obtain such fragments. There is no guidance as to what the biologically-active and immunogenic fragments are; or what fragments can or cannot be used in the complex being claimed. The specification does not include structural examples of biologically-active and immunogenic fragments. Thus, the resulting fragment could result in a complexes not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically identified sequences, the skilled artisan cannot envision the detailed structure of the fragments, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative

Furthermore, claim 8 is drawn to an isolated polynucleotide comprising a sequence selected from a) a polynucleotide sequence of SEQ ID NO:2; b) a naturally-occurring polynucleotide sequence having at least 90% sequence identity to SEQ ID NO:2; c) a polynucleotide sequence complementary to a); d) a polynucleotide sequence complementary to b); and e) a ribonucleotide equivalent of a)-d).

The claims drawn to the polynucleotides fail to recite any associated function. Without an associated function there is no limit on the polynucleotides encompassed by applicants claims. It is noted that there is no requirement that the polynucleotides have glutathione S-transferase activity, therefore any single polynucleotide that is complementary or any single ribonucleotide meets the limitations of the claims. Furthermore any variant or mutant that has similar sequence identity yet has a different function is also encompassed by the claims. However, applicant has not taught examples of such polynucleotides and ribonucleotides. Thus, the structure of sequences or complementary polynucleotides that encode a polynucleotide having sufficient glutathione S-transferase activity have not defined and broaden the scope of the invention to encompass polynucleotides not described by the instant specification.

Sections b), c) and d) of claim 8 are drawn to an isolated polynucleotide comprising b) a naturally-occurring polynucleotide sequence having at least 90% sequence identity to SEQ ID NO:2; c) a polynucleotide sequence complementary to a); or d) a polynucleotide sequence complementary to b).

Sequences having 90% identity to either SEQ ID NO:2 or complementary

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The specification only discloses SEQ ID NO: 2, there is no disclosure of nucleotide sequences with 90% identity of SED ID NO: 2 or complementary sequences comprised within the family of enzymes. Thus, the structure of these nucleic acid molecules or polynucleotides is not defined. Even though the claims recite a sequence identification number, the skilled artisan cannot envision the detailed structure of the encompassed nucleic acid molecules since the specification has not defined what the 10% variables can be. Moreover, a skilled artisan cannot envision the detailed structure of complementary sequences. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

The claims fail to recite the precise definition of the nucleic acid sequence with at least 90% identity to SEQ ID NO:2, and the associated complementary sequences or an

claims which lack a function of the polynucleotides are insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645. Therefore, the full breadth of the claims fails to meets the written description provision of 35 USC 112, first paragraph.

8. Claims 2-4 and 8-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In particular, sections of claim 8 (e-g) drawn to an isolated polynucleotide comprising b) a naturally-occurring polynucleotide sequence having at least 90% sequence identity to SEQ ID NO:2. However absent factual evidence, a percentage sequence similarity of less than 100% is not deemed to reasonably support, to one skilled in the art, as to whether the biochemical activity of the claimed subject matter would be the same as that of such a similar known biomolecule. It is known for nucleic acids as well as proteins, for example that even a single nucleotide can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Moreover, it is well known that ~~that~~ a single nucleotide insertion will downshift the reading of the sequence and can result in a polynucleotide encoding a

unpredictable and therefore unreliable correspondence between the claimed biomolecules and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement.

Several publications document the unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as well as noting certain conserved sequences in limited specific cases: Russell [J. Mol. Bio.244:332-350]; Skolnick et al., [Trends in Biotech, 18(1):34-39]; and Attwood, [Science, 290:471-473, (29 October 2000)].

In absence of further guidance from Applicants, the skilled artisan would have to de novo discover what the appropriate conservative amino acid substitutions are and what critical regions can and cannot tolerate such substitutions. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. The need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use for bacterial membrane polypeptides. Therefore, a skilled artisan would be forced into undue experimentation to practice (i.e., make and use) the invention as is broadly claimed.

9. Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

Claim 2 recites the limitation "an isolated polynucleotide encoding a polypeptide"; and claim 3 recites the limitation "a recombinant polynucleotide" however claim 1 does not recite a polynucleotide. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claim 8 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-4 of U.S. Patent No.5,817,497. Although the conflicting claims are not identical, they are not patentably distinct from each other because

Claim 8 of the instant application is drawn to an isolated polynucleotide comprising a sequence selected from a) a polynucleotide sequence of SEQ ID NO:2; b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to

SEQ ID NO:2; c) a polynucleotide sequence complementary to a); d) a polynucleotide sequence complementary to b); and e) a ribonucleotide equivalent of a)-d).

Claims 3-4 of US Patent 5,817,497 are drawn to an isolated and purified polynucleotide comprising SEQ ID NO:2; a polynucleotide sequence complementary to SEQ ID NO:2; and a host cell containing an expression vector that contains the polynucleotide. The claims 3 and 4 of US Patent 5,817,497 is drawn to the same polynucleotide or complementary polynucleotide as claimed in instant claim 8 a) and 8 c). It is noted that SEQ ID NO:2 of the instant application is identical to SEQ ID NO:2 of US Patent 5,817,497. Thus, the polynucleotides are not patentably distinct.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 8-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al., (Accession Number H27975). Hillier et al., teach a human cDNA clone that is similar to mouse glutathione S-transferase GST. There are stretches of nucleic acids within the sequence that are complementary to SEQ ID NO:2. Moreover the sequence of Hillier et al., recites a polynucleotide comprising at least 60 contiguous nucleic acids.

be complementary; i.e., there is no requirement of fully complementary. Thus one complementary nucleotide meets the limitations of the claims.

Therefore, Hillier et al., teach the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 2-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier et al., (Accession Number H27975) in view of Simula et al. Hillier et al., has been discussed above, however Hillier et al., does not disclose recombinant transformed cells comprising promoters.

Simula et al., developed *Salmonella typhirumurium* strains that express human glutathione S-transferase (GST) (abstract). The GST was expressed using regulatable *tac* promoter expression systems (abstract).

Therefore, it would have been prima facie obvious to modify the cell transformed with a recombinant polynucleotide as taught by Simula et al., with the polynucleotide of Hillier et al. One would have a reasonable expectation of success since both polynucleotides sequences are drawn to human glutathione S-transferase and no more

would have been motivated to use alternative and functionally equivalent sequences since only the expected expression would have been obtained. Moreover, the prior art clearly teaches skilled artisans would have had a reasonable expectation of success in switching the sequences since the use of alternative and functionally equivalent sequences would have been desirable to those of skill in the art.

Prior Art

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Stenberg et al. (Vol. 3, 1992) teach heterologous expression of glutathione transferase.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.